Original Article

Biological parameters influencing the human umbilical cord-derived mesenchymal stem cells' response to retinoic acid

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Abstract

Human umbilical cord-derived mesenchymal stem cells (HUCMSCs) are multipotent fetal stem cells that differentiate into various cell lineages. In recent years, they have gained attention for therapeutic applications but very little is known about their sensitivity to chemical agents such as widely used retinoic acid (RA). As a morphogen inducing differentiation of mesenchymal stem cells, RA has for a long time been known to be a potent teratogen promoting craniofacial and limb abnormality in vertebrate embryos. Here, using MTT assay and EB/AO staining as well as TUNEL assay we show that RA in a concentration-dependent manner induces apoptosis through upregulating *Caspase* expression and increasing *Bax/Bcl2* ratio. Moreover, different biological parameters such as initial time seeding, cell density, passage number and duration of RA treatment play a major role in HUCMSCs cytotoxic response to this agent. © 2014 BioFactors, 00(00):000–000, 2014

Keywords: *human umbilical cord-derived mesenchymal stem cells; apoptosis; retinoic acid; cytotoxicity*

1. Introduction

Human umbilical cord contains a mucoid matrix, Wharton's jelly, surrounding two arteries and a single vein. It is characterized by loosely arranged cells embedded in proteoglycan-rich connective tissue that nourishes them. These easily accessible cells, also termed human umbilical cord-derived mesenchymal stem cells (HUCMSCs) are fetal stem cells with self-renewing abilities and resemble morphologically to fibroblast cells [1–3]. They are typically considered to be multipotent cells, since they can differentiate into various cell types including neural cells, osteocytes, and hepatocytes [4–6]. Compared with other mesenchymal stem cells, HUCMSCs interestingly do not express major histocompatibility complex (MHC) class II, which can elicit an immunity response in transplant recipients. These features make them a promising source for clinical cell replacement therapy [7–10].

Retinoic acid (RA), an active derivative of vitamin A, is one of best known molecules to play a fundamental role in vision, the immune system, reproduction, apoptosis, differentiation, and proliferation of cells and as a biological morphogen regulates normal embryonic development. These functions of RA are mediated through two classes of receptors, RAR and RXR

Volume 00, Number 00, Month/Month 2014, Pages 00–00
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Received 21 July 2014; accepted 2 November 2014
DOI 10.1002/biof.1192
Published online 00 Month 2014 in Wiley Online Library (wileyonlinelibrary.com)